Shine Your Eyes: Technology, Policy, and a Need for Vigilance in Detecting Counterfeit Antimalarials in Sub-Saharan Africa

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Shine Your Eyes: Technology, Policy, and a Need for Vigilance in Detecting Counterfeit Antimalarials in Sub-Saharan Africa*

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Abstract

Malaria remains a significant global health problem, despite continued efforts made for its eradication. Nearly half of the world’s population lives in malaria-endemic regions, with the burden resting primarily in low- and middle-income countries in sub-Saharan Africa. Malaria and the costs of treatment trap families in a cycle of illness, suffering, and poverty. Despite the efficacy of malaria treatments, malaria remains highly virulent due to the prevalence of substandard and falsified medicines. For decades, drug counterfeiting has remained underestimated and ignored, though fraudulent pharmaceuticals are on the rise in many countries because, simply put, it is a profitable business and there is high demand, particularly for lifesaving drugs such as antimalarials. These medicines, which may be produced or distributed deliberately or unintentionally, neither prevent nor cure malaria in the individuals who take them and often cause significant adverse effects and premature death. They can also cause the parasite to develop drug resistance, which is especially dangerous for those living in malaria-endemic countries.

However, there are ways in which countries can stem the importation, production, and dissemination of fraudulent antimalarials. In this report, we will first outline the problem at hand before diving into a case study of Nigeria, an impressive example of how to reduce the prevalence of substandard and falsified pharmaceuticals in a given country. We will then finish the report by discussing, at a high level, what remains to be done to continue making strides toward malaria eradication.

Keywords: counterfeit, substandard, falsified, antimalarial, malaria, pharmaceuticals, Africa, Nigeria

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1. Introduction

In spite of tremendous efforts made for its eradication, malaria remains a major global health problem. It is still a leading cause of morbidity and mortality with severe public health and economic impacts; however, the burden of the disease rests primarily in low- and middle-income countries. According to the latest WHO data, in 2018, there were an estimated 228 million cases of malaria worldwide, 93% of which were in the WHO African Region (which encompasses all countries in Africa except Sudan, Somalia, Egypt, Libya, Tunisia, and Morocco) (World Health Organization, “WHO African Region Country Offices”). In fact, six countries in sub-Saharan Africa accounted for 54% of cases worldwide – Nigeria (25%), Democratic Republic of the Congo (12%), Uganda (5%), and Côte d’Ivoire, Mozambique, and Niger (4% each) (“World Malaria Report,” 2019).

In 2018, an estimated 405,000 people died of malaria, with over 94% of these deaths occurring in the WHO African Region. Six countries in sub-Saharan Africa accounted for 52% of all global malaria deaths – Nigeria (24%), Democratic Republic of the Congo (11%), the United Republic of Tanzania (5%), and Angola, Mozambique, and Niger (4% each). Children under five years are at the highest risk of contracting and dying from the disease – in 2018, they accounted for 67% of all malaria deaths (Cartwright and Baric, 2018; “World Malaria Report,” 2019). This translates into a daily toll of over 745 children under the age of five.

Looking beyond public health impacts, malaria is a substantial economic burden as well. Since 2000, malaria has cost sub-Saharan Africa US$ 300 million each year for case management alone and is estimated to cost up to 1.3 percent of GDP in all of Africa (United Nations Children’s Fund, 2018).

Despite these numbers, there is progress being made in reducing the number of deaths from malaria. In 2018, an estimated US$ 2.7 billion was invested in malaria control and elimination efforts globally by governments of malaria-endemic countries and international partners (albeit, a reduction from the US$ 3.2 billion invested in 2017, and falling short of the US$ 5 billion estimated to be required globally to stay on track). Nearly three quarters of investments were spent in the WHO African Region (“World Malaria Report,” 2019). In most African countries, substantial malaria-control activities have been implemented, including the widespread deployment of long-lasting insecticidal nets, the use of indoor residual spraying of insecticides, prompt diagnosis using rapid diagnostics tests, and treatment with highly effective artemisinin-based combination therapies (ACTs) (World Health Organization, 2016). These interventions are highly cost-effective and associated with reduction of incidence rates of malaria and malaria deaths (O’Meara et al., 2010). Specifically, the combination of prompt diagnosis and treatment remains the most effective way to prevent malaria from developing into severe disease and
death. If an infected patient is diagnosed early, treatment is nearly 100% effective when properly prescribed and administered (Nabarro and Mendis, 2000; “World Malaria Report,” 2019).

That being said, obtaining authentic and unexpired antimalarials is more difficult than one may think, or hope, due to the prevalence of counterfeit medicines in many malaria-endemic countries. While definitions of “counterfeit” vary worldwide, the most commonly used definition was put forth by the WHO in 2017, defining “counterfeit” pharmaceuticals as falsified, substandard, and unregistered/unlicensed medicines. As a result, the term “counterfeit” has been phased out in recent years and replaced with the more specific “substandard and falsified”, also abbreviated as “SF” (World Health Organization, 2017; World Health Organization, 2017b). For the remainder of this report, pharmaceuticals that fall into any of the aforementioned categories will be referred to as “SF”.

Much of the morbidity and mortality associated with malaria could be avoided if drugs available to patients were efficacious and high quality. The use of poor-quality or fake medications often provokes serious complications and, in many cases, premature death. The subtherapeutic nature of poor-quality medicines in particular contributes to increasing drug resistance, especially to chronic infectious diseases such as malaria (Ayukekbong et al., 2017). The prevalence of SF drugs also has financial consequences for patients, their families, and healthcare systems due to additional treatment-seeking, further care, and increased morbidity and mortality. Patients and their households lose income and productivity, the effects of which are felt by businesses and the broader economy (Beargie et al., 2019). Pharmaceutical companies producing genuine products lose business. All of this culminates in a lack of social mobility and increased poverty in the regions most affected by the SF drug trade.

Research findings clearly show that the poorest, most vulnerable populations suffer the most – recent research estimates that 1 in 10 products circulating in low- and middle-income countries is either substandard or fake (World Health Organization, 2017a). While higher-income countries offer a more lucrative market for SF drugs, they also have the most advanced technologies and regulatory bodies in place for combatting them. In contrast, the poorest third of WHO member states, many of which are in sub-Saharan Africa, have either no means or very limited means of controlling SF medicines (“Assessment of medicines regulatory systems in sub-Saharan African countries: An overview of findings from 26 assessment reports”; Kelesidis et al., 2007; World Health Organization, 2018). Counterfeiters prey on lower-income countries due to the unfortunate confluence of struggling economies, weak technical capacity, limited regulatory oversight, a lack of punitive action, a preponderance of poor consumer and health-worker knowledge about product authenticity, and a large, unregulated private sector for purchasing drugs.

High burden of disease is another reason why there is such a large market for criminals to produce SF drugs in sub-Saharan Africa. The high prevalence of malaria generates a constant, high demand for antimalarials. Various studies estimate that one-third of antimalarials in sub-Saharan Africa are fraudulent, causing anywhere between 72,000 to 267,000 deaths every year.
Global achievements in reducing malaria-related deaths in the past decade are in danger of significant reversal if the problem of SF drugs continues, particularly in sub-Saharan Africa, where billions have been spent to create sustainable malaria-control programs.

Despite the fact that the true scale and impact of the SF antimalarial trade may be unknowable at this point in time, it is well understood that SF antimalarials do exist in many malaria-endemic countries. In this paper, we plan to dive into how SF antimalarials infiltrate the market, where the primary pain points are in the supply chain from the manufacturer all the way to the consumer, and what national governments and individuals can do in order to stem the tide of SF antimalarials and combat this epidemic.
2. Substandard and Falsified Medicines

Before delving too deeply into the material, it is important to discuss not only what qualifies as “counterfeit” but also what the estimated scale and impact of the fraudulent antimalarial trade is in sub-Saharan Africa, where the burdens of both the disease and the drug trade are most prevalent.

Definitions

There are several ways in which “counterfeit” has been defined over the years. In fact, this is one of the reasons it is so difficult to assess the true scale of the counterfeit drug trade – different agencies and regions have varying definitions for “counterfeit”, “substandard”, “falsified”, and other similar terms (World Health Organization, 2017). However, the most widely used definition was put forth in 2017 by the WHO. These definitions indicate that “counterfeit” includes falsified, substandard, and unregistered or unlicensed medical products, with definitions as follows (World Health Organization, 2016b; World Health Organization, 2017c):

- **Falsified** medical products are those that deliberately or fraudulently misrepresent their identity, composition, or source; these products are produced and distributed with criminal intent.
- **Substandard** medical products are issued by national regulatory authorities but fail to meet national or international quality standards or specifications; these products frequently have low active pharmaceutical ingredients or dissolution properties.
- **Unregistered or unlicensed** medical products are those that have not been assessed or approved by the national or regional regulatory authority for the market in which they are distributed.

In addition, degraded products are those in the aforementioned categories that have chemically broken down, either due to improper storage, expiration, or adverse climatic conditions (Risha et al., 2002).

Scale

In spite of its global nature, the SF pharmaceutical trade does not affect all parts of the world equally. The WHO estimates that SF drugs account for up to 30% of drug sales in sub-Saharan Africa but only 1% in middle- and high-income countries (World Health Organization, 2006b). Even still, the issue may be much more extensive than it seems due to the inherent underground nature of the business. Measuring the magnitude of the phenomenon becomes exceedingly complicated, particularly due to the number of those involved in production and distribution, disposable means used to detect trafficking routes, and the difficulty in coordinating information collected from various stakeholders (“Counterfeit Medicines and Organised Crime”).
Intelligence reports have indicated that SF drug products change hands more than 30 times before reaching final buyers, showing that those involved in the trade go to great lengths to conceal the origin and path of their products (Lewis, 2009).

That being said, it is well-known that SF pharmaceuticals in sub-Saharan Africa typically come from one of three sources: (1) abroad, predominantly China or India, (2) neighboring countries in sub-Saharan Africa, with drugs either being smuggled across borders or being imported legally, or (3) domestic manufacturers. Once these SF drugs make it to the consumers, most cases are likely unreported, reported to the wrong agencies, or kept confidential by pharmaceutical companies not wanting to tarnish their reputations (Basco, 2004; Newton et al., 2001; Newton et al., 2006). In sub-Saharan Africa specifically, countries offer minimal or no reporting on the incidence of SF drugs, which, again, paints an unrealistic picture of a rather dire situation. Due to all of these confounding factors, there are no reliable global estimates available describing the prevalence of SF medicines. It is well-documented that even the most formal reports quantifying economic impact and scale are based on rough estimates (Spink and Fejes, 2012; U.S. Government Accountability Office, 2010).

Impact

Regardless of the scale of the issue, SF antimalarials have tremendous health, economic, and socioeconomic impacts in sub-Saharan Africa. Health impacts include increased morbidity, mortality, and disease prevalence, along with the progression of drug-resistant infections (White, 2008; World Health Organization, 2010). While numbers vary, one study estimates up to 155,000 childhood deaths worldwide every year due to falsified antimalarials (Renschler et al., 2015). Another study estimates an additional 529 deaths per 1 million malaria cases, amounting to an additional 72,000 to 267,000 deaths per year in sub-Saharan Africa (World Health Organization, 2017). The WHO estimates that SF antimalarials cause up to 20% of malaria deaths worldwide (Karunamoorthi, 2014). Despite the fact that estimating the number of deaths due to SF antimalarials is intricate and complex beyond measure, studies clearly show that this trade has a colossal impact on public health. The presence of SF medicines also leads to a loss of confidence in healthcare professionals, health programs, and health systems (Newton et al., 2010). This is significant as it can result in patients deciding to forgo treatment altogether and/or seeking alternative treatment from unregulated outlets and/or care providers, leading to further adverse events (Bloom et al., 2008; Institute of Medicine, 2013; Newton et al., 2010).

Economic impacts include increased out-of-pocket and health system spending and economic loss for patients, their families, health systems, and the manufacturers and traders of quality medicines. The total annual economic impact of SF antimalarials is estimated at US$ 12 billion in direct losses (Karunamoorthi, 2014), and the incurred cost due to additional treatment-seeking and further care specifically is estimated at roughly US$ 12.1 million and US$ 52.4 million. SF medicines also increase the burden for healthcare professionals, regulatory agencies, customs officials, law enforcement, and criminal justice systems, further straining already overworked
systems (Newton et al., 2010; World Health Organization, 2017). All of this culminates in a lack of social mobility and increased poverty in the countries most affected.

**A Soft Target**

There are many factors that contribute to the production and sale of poor-quality antimalarials. In many malaria-endemic countries in sub-Saharan Africa, there is an unfortunate confluence of weak regulation, a lack of punitive action, high demand, and a preponderance of poorly educated healthcare workers and consumers, all of which help to create a porous system (Nayyar et al., 2012; Renschler et al., 2015; Zaman, 2018).

There is very limited regulatory oversight and quality control, and, without sufficient legal oversight, the system is left unchecked (Nayyar et al., 2015). The WHO estimates that 30% of countries, most of which are in sub-Saharan Africa, lack any capacity to oversee medicine manufacture, importation, or distribution (Kelesidis et al., 2007; Renschler et al., 2015). Despite many countries in sub-Saharan Africa technically having National Medicine Regulatory Authorities (NMRAs), per the WHO’s suggestion, many of them are not operating effectively enough to prevent SF medicines from infiltrating the supply chain (“Assessment of medicines regulatory systems in sub-Saharan African countries: An overview of findings from 26 assessment reports”; World Health Organization, 2018). A survey of 26 NMRAs in 26 sub-Saharan African countries indicated a lack of sustainable funding, a shortage of qualified staff, and few or no operational resources. Specifically, 21 of the 26 bodies had either inadequate or no quality-monitoring programs in place to detect SF medicines. The WHO also recommends that all NMRAs should have specific programs capable of differentiating between falsified and substandard medicines; however, only five of the 26 NMRAs had implemented these, and none met the WHO’s guidelines (“Assessment of medicines regulatory systems in sub-Saharan African countries: An overview of findings from 26 assessment reports”). The notable absence of a regulatory structure in many countries inevitably creates a chaotic drug distribution network and a large, unregulated private sector for purchasing pharmaceuticals in which illegal drugs are easily imported, unqualified vendors are common, and small pharmaceutical companies with no quality assurance abound.

There is also a dire lack of appropriate drug legislation, enforcement of existing laws, and penalties. The root of this problem may stem from inconsistencies in national penalties for counterfeiting medicines and the overall lack of an international legal framework in what is increasingly becoming a global trade (Attaran et al., 2011; Nayyar et al., 2012). In some countries, counterfeiting is not considered a crime, while in other countries, the penalty is death (Harris et al., 2012). Most countries, particularly those most affected by the SF drug trade, do not have laws that are strong enough or systems that are efficient enough to prosecute criminals. Implementation of current legislation is lax due to a scarcity of political will and competing law enforcement priorities. On the rare occasion authorities catch counterfeiters, the time between seizure of poor-quality medicines and a trial can be two or more years (Commission of the US
FDA, 2014; Zaman, 2018). Often, after long litigation, the sentence is lighter than those handed down to criminals involved in other illegal trades. Penalties are not commensurate with the severity of the crime, and, when compared to the profit generated by SF medicines, the business still remains highly lucrative.

A high disease burden makes for steady constant demand, and, when paired with a paucity of regulatory and punitive action, this makes for a profitable SF market with few-to-no barriers to entry. Up to 90% of people living in sub-Saharan Africa have to pay for essential medicines of some kind (Cameron et al., 2009); more specifically, over 90% of worldwide malaria deaths occur in Africa, which makes for an exceedingly high demand for antimalarials (“World Malaria Report,” 2019). Genuine drugs are inaccessible and expensive, particularly since the WHO changed official guidelines for treating malaria in 2006 from chloroquine to ACT. Although ACT is more efficacious, it costs between five and 23 times more to manufacture, which means the drug is significantly more expensive for patients to purchase (O’Connell et al., 2011). Those patients with limited resources who pay out of pocket fall victim to the SF drug trade because the cost of the genuine product is out of reach, so they choose a less expensive medicine available, which is typically substandard or falsified (Bate, 2008). Many patients are unaware of the danger of buying inexpensive drugs, which segues into the final facet that makes Africa an easy target – a lack of knowledge or awareness surrounding product authenticity. A study in Tanzania reported that 96% of people did not know that drugs could contain concentrations of ingredients that were lower than advertised (Jande et al., 2000). Even those patients who are aware of the correlation between reduced cost and lower quality may be willing to overlook this if the price is low enough and the need is high enough.

Patients are not the only ones who are uninformed about the imminent danger of SF antimalarials – healthcare workers, specifically pharmacists, are largely unaware as well when it comes to product authenticity. Pharmacists are viewed as the gatekeeper, those charged with final custody before dispensing medicines to patients. They are also tasked with ensuring proper use and administration of medicines. However, a review of the national pharmacy curricula in eight countries, six of which were in sub-Saharan Africa, found that only one specifically mentioned training in SF medicines. Even when training on the topic is included, it is typically limited to elective modules rather than integrated into the core curricula (Ferrario et al., 2019). This leaves very few pharmacists who are properly trained in SF medicines, whether it is the danger, the prevalence, or how to identify and subsequently report these medicines when found in their stock.

For all of these reasons, many low-income countries in sub-Saharan Africa make for a highly lucrative market for fraudulent pharmaceuticals with few barriers to entry. Due to the sheer number of factors at play, interventions must come at several points throughout the supply chain and must be multidisciplinary in nature. There is no single silver bullet solution for such a complex and intricate problem.
3. Nigeria Case Study: Background

Nigeria has been at the forefront of establishing policies to eradicate SF medicines since the early 2000s. Nigeria is the single most heavily malaria-burdened country in the world with 48 million clinical episodes and 180,000 deaths per year, making for a ripe SF antimalarial drug market (Kaur et al., 2015). Here, we will detail the problem, what prompted Nigeria to take action, what steps were taken, and the achievements of this multi-layered campaign. Specific measures put in place will remain high-level in this section and be more fully detailed in the next.

While discussing the prevalence of SF drugs in Nigeria, it is important to note that, while Nigeria has one of the highest recorded quantities of SF medicines in sub-Saharan Africa, this is likely due to the fact that Nigeria is also home to one of the largest economies in the region (International Monetary Fund, 2019). As such, even a small percentage of SF medicines would translate to a relatively high quantity of seizures. Additionally, increased enforcement action often highlights the extent of a problem while many countries have no ability or desire to look for SF drugs, which may artificially reduce the perceived scale of the SF pharmaceutical market in these countries.

The Problem

During the 1990s, Nigeria had the largest market of SF pharmaceuticals in the world (Bate, 2008). In 1987, a nation-wide study of the quality of Nigeria’s pharmaceuticals found that 70% of drugs in the country were falsified (Bird, 2007). To address this problem, the National Agency for Food and Drug Administration and Control (NAFDAC) was formed in 1994, though it was ineffective in its first several years due a combination of inadequate infrastructure and a lack of political will to properly enforce legislation and standards (Garuba et al., 2009). In 1998, NAFDAC introduced Decree No. 21, which criminalized the manufacture, sale, and distribution of counterfeit, adulterated, banned, and fake drugs in open markets and without a license of registration (Akinyandenu, 2013). However, again, there was little-to-no positive effect due to derisory infrastructure and a deficiency of political willpower and enforcement.

At the turn of the century, the problem reached dramatic proportions. In 2001, SF medicines still accounted for approximately half of all available drugs in Nigeria. Around this time, Cameroon and Niger banned the sale of Nigerian-manufactured pharmaceutical products due to their poor quality, which subsequently caused investments to fall and the Nigerian economy to weaken. A NAFDAC survey found that 68% of drugs in the country were unregistered and, therefore, likely substandard or falsified (World Health Organization, 2006). All of this is what ultimately prompted Nigerian authorities to take action (Bate, 2008).
Action Taken

Nigerian anti-counterfeiting measures began in 2001 and continue to evolve nearly two decades years later. In 2001, the Nigerian president overhauled NAFDAC and installed Dr. Dora Akunyili as the director general of the agency. The aim of restructuring the organization was to “safeguard the health of the nation” (Akinyandenu, 2013). The first step NAFDAC took was rooting out corrupt inspectors within its own ranks, and drug seizures immediately skyrocketed. For example, in 2004, a raid found 3,000 unregistered medicine outlets. Another raid in 2008 was made on a large market, resulting in the seizure of 80 truckloads of SF medicines (Orszag-Land, 2008). Between April of 2001 and January of 2006, NAFDAC seized and destroyed substandard products valued at approximately US$ 100 million (Akunyili, 2006). As recently as 2016, NAFDAC seized more than US$ 33 million and destroyed more than US$ 5 million worth of SF drugs over the course of the year (This Is Africa, 2017).

Other efforts focused on securing the border and increasing awareness among the public. The central government closed the majority of the border to pharmaceutical imports while increasing surveillance at the remaining access points. A public awareness campaign helped educate consumers on the prevalence of SF medicines, as well as how to identify and report them to the appropriate authorities. More details on specific countermeasures put in place to fight the SF pharmaceutical trade will be discussed in upcoming sections.

Achievements

NAFDAC has been recognized for their impressive advancements as a global leader in the fight against fake and substandard medicines. Some sources say that the prevalence of SF medicines decreased from 67% in 2001 to 16% in 2004 (World Health Organization, 2006); others say that SF drug circulation dropped by over 80% between 2001 and 2006 (Akinyandenu, 2013). A study conducted in 2005 by NAFDAC in collaboration with the WHO and the UK’s Department for International Development revealed that prevalence dropped from 40% in 2001 to 16.7% in 2005. Several studies have been conducted in the last ten years to test the quality of medicines with various devices, and each study has shown that over 95% of samples tested pass various quality measurements (Adyeye, 2019). Between 2001 and 2004, the quantity of unregistered drugs, or drugs that had not been cleared by NAFDAC for importation, had fallen by 80% (World Health Organization, 2006). Though exact statistics slightly differ, again due to the inherent nature of the business and the difficulty in accurately quantifying the scale, the key takeaway remains – Nigeria has been largely successful in reducing the prevalence of SF pharmaceuticals.

These significant decreases have brought about tangible public health and economic benefits. By 2006, other West African countries had lifted bans on drugs manufactured in Nigeria. Production capacities of domestic pharmaceutical companies increased, and dozens of new drug manufacturing outfits were established between 2001 and 2010 (Akunyili, 2006). Countless lives
have been saved. Because of NAFDAC’s admirable achievements in stemming the tide of SF medicines, much of what we discuss in the remainder of this paper comes from NAFDAC’s work in this vein.

Nigeria has taken a multi-layered approach to solving the problem of SF medicines. The Nigerian government has realized that single-faceted, domestic solutions alone cannot solve this transnational problem. Interventions must be placed at multiple nodes along the supply chain, and these interventions must span multiple domains in order to effectively curb the presence of SF pharmaceuticals.

NAFDAC has put countermeasures in place at the drug source (both international and domestic), at the Nigerian border, at a national level, and on a local, individual level. These countermeasures range from improving surveillance at entry points for imports, establishing partnerships with exporting countries to reduce the prevalence of fraudulent medicines at the source, increasing punishments for convicted criminals, and raising public awareness around the issue (Akunyili, 2004). We will now break down the specific actions taken at each point in the pharmaceutical supply chain.

At the Source

Engaging source economies, whether international or domestic, can significantly reduce the supply of SF medicines. India and China are Nigeria’s largest importers of medicines, and, in 2011, the European Commission estimated that Indian exports were responsible for ¾ of the SF drugs in Nigeria (Chika et al., 2011). NAFDAC accordingly established contacts and programs with both India’s and China’s national governments in an effort to restrict the in-flow of SF medicines from these countries. Trade and health negotiations between the countries allowed for Nigerian officials to conduct random inspections of manufacturing plants and pre-inspections of products before being exported (Akinyandenu, 2013; Financial Express, 2009; Spink et al., 2016). NAFDAC appointed foreign analysts in India, China, and Egypt to conduct these audits and to re-certify drugs before exportation. NAFDAC has focused many efforts on working specifically with Indian authorities, and, in turn, India has provided many of its own resources to the cause since the early 2000s. In addition to cooperating with Nigerian officials, the Indian government also sends NAFDAC updated lists of specific blacklisted pharmaceutical companies to prevent these products from being bought (Akinyandenu, 2013; Raufu, 2003). All of these engagement strategies have resulted in multiple criminal convictions of counterfeiters in both India and China (All Africa, 2009).

While these approaches work to stem the production of SF medicines internationally, distinctly separate strategies are needed domestically. Within the country, authorized drugs are required to carry a NAFDAC registration number, which enables pharmacists and consumers to more readily identify which medications have been verified and by whom. NAFDAC also
conduits random audits and inspections of local drug manufacturers for quality assurance purposes.

There are some limitations to only staging interventions at the source. Fraudulent products from abroad can still slip through the export and import detection and deterrence programs. In addition, this approach relies heavily on cooperation between countries and efficacy of detection measures. This is why engaging source economies is but one facet of a successful approach.

**At the Border**

In many cases, lax law enforcement at customs’ points can allow SF medicines to penetrate a country’s supply chain. To combat this, NAFDAC implemented tighter and more effective surveillance at all points of entry and enhanced enforcement activities. Specifically, in 2003, NAFDAC banned the importation of any and all drugs apart from those arriving at two ports and two airports. This allowed NAFDAC to focus all measures to check legitimacy of drug imports in these four areas. Between 2003 and 2009, Nigeria customs officials destroyed approximately US$ 109 million worth of SF drugs (Bate, 2008). In an effort to further improve customs officials’ ability to analyze drugs entering the country, in 2011, NAFDAC purchased 100 GPHF-Minilabs and distributed them to officials at the border. A Minilab is a portable field screening kit capable of providing semi-quantitative information on the active pharmaceutical ingredients present in a sample. These devices enabled officials to quickly test drugs entering the country at the border without needing to send samples to a central laboratory (Akinyandenu, 2013). Since then, TruScan devices have also been broadly distributed at the border to detect SF medicines (Egwu, 2017).

**At the National Level**

At the national level, NAFDAC has taken a truly multidisciplinary approach to problem-solving with actions spanning legislation, regulation, and the media.

NAFDAC has created legislation and significantly strengthened enforcement since the late 1990s and early 2000s in an effort to deter fraudsters. Public support for better enforcement and stricter punishments increased after the Chinese and Indian governments implemented life imprisonment sentences and death penalties for counterfeiters exporting to Nigeria (All Africa, 2009; Spink et al., 2016). Nigeria now has more than 11 laws related to drugs, poisons, food control, product registration, and adulteration. Nigeria also implemented tougher sentencing, including life imprisonment and higher fines. Prior to Dr. Akunyili’s appointment within NAFDAC, someone convicted of drug counterfeiting could be fined no more than 5,000 Nigeria Naira (roughly equivalent to US$ 14 today). This did very little to deter criminals given the profits to be gained from the trade. Shortly after her appointment, Dr. Akunyili passed a law that increased the fine to 500,000 Nigeria Naira (roughly equivalent to US$ 1400 today) (Akunyili, 2004). The hope was that, given Nigeria’s GDP per capita, the hundred-fold increase in the fine would strongly discourage counterfeiting (Attaran et al., 2011). These legislative actions resulted
in 45 convictions for drug counterfeiters in 2006, with another 56 pending trial, which is claimed to be more than those charged in the previous decade (Akunyili, 2004).

NAFDAC also made distinct efforts to regulate supply chains in order to control the distribution of authentic medicines and improve quality of service. As was mentioned previously, NAFDAC now requires authorized drugs to carry a registration number, and the Nigerian Task Force conducts both routine and surprise inspections, as well as inspections upon receiving complaints, at manufacturing facilities to ensure quality. In 1999, Decree No. 25 granted additional power to the Nigerian Task Force to close down all unregistered premises and open drug markets, in coordination with NAFDAC officials.

On the regulatory side, there have been clear advances made in creating a well-defined, primary, traditional market as drug distribution in Nigeria has historically been described as “chaotic” (Akunyili, 2004). This initiative includes:

- creating a central medicine distribution network of warehouses,
- allowing only registered pharmacies to sell medicines, and
- allowing only certified pharmacists to dispense product (Business Monitor International, 2010).

The goal is to strengthen Nigeria’s medicine distribution system and deter sellers from knowingly selling SF products due to a risk of losing their certificates. Unfortunately, there is still the reality that patients who cannot afford the medicines available in the primary supply chain will seek out medicines elsewhere, typically from less legitimate sources. However, Nigeria has taken and continues to take meaningful steps to improve and strengthen the primary supply chain.

Lastly, there has been a media push to consider pharmaceutical counterfeiting on par with trafficking of illicit drugs, such as cocaine and heroin. Weak penal sanctions are a major factor in the proliferation of SF drugs – even on the rare occasion authorities catch criminals involved in the SF drug trade, they tend to receive lighter penalties than those involved in other illegal trades, specifically the trafficking of illicit drugs (Bate, 2008). Antimalarials are a lifesaving drug, and to knowingly manufacture and/or distribute SF antimalarials is a crime with much more impactful, debilitating consequences than that of illicit drug trafficking. Therefore, efforts are being made to more closely align penalties with the severity of the consequences.

At the Individual Level

The final, arguably most important, interventions occur at the individual consumer level. Increasing awareness, implementing innovative technologies, and revamping the pharmacists’ education system are the primary thrusts at this level.

Increased consumer awareness of SF medicines reduces the number of patients who fall victim to these drugs. NAFDAC aims to empower the public through local and national media.
As mentioned previously, the media is used to improve legislation while also raising awareness of this widespread problem.

Innovative technologies have also enabled both companies and consumers to become directly involved in efforts to identify and report SF medicines, both at the point of purchase and further upstream. Consumer serialized codes, such as those created by the company Sproxil, enable consumers to authenticate a product through a bar code using a mobile phone. The bar code is masked by a scratch-off feature, making it easy to determine if the bar code has been tampered with prior to the patient’s verification. Other companies, such as mPedigree, take it one step further and allow manufacturers and regulators to monitor the supply chain, pinpointing the weak points where SF pharmaceuticals are entering the system. While there are countless different technologies that could be used in this sphere, the most mature digital anti-counterfeit technologies have proven to be mobile and RFID-based solutions, which enable more robust detection, authentication, and track-and-trace (Mackey and Nayyar, 2017).

Education for pharmacists has also been a recent focus as pharmacists play an integral role in protecting the supply chain from SF pharmaceutical products. They are the last point of contact before medicine is handed over to the patient, and they are presumed experts in the field. However, prior to 2004, the only academic requirement for community pharmacists was a secondary school-leaving certificate, which did not equip them to identify or report SF drugs in their stock (World Health Organization, 1999). In 2004, NAFDAC increased the length of training required for community pharmacists, adding a specific module focused on (1) identifying SF drugs using a range of tools and technologies, and (2) reporting these drugs to the appropriate authorities (Akinyandenu, 2013). Separately, the International Pharmaceutical Federation is collaborating with the WHO to pilot an education component on SF medicines in four African countries (Ferrario et al., 2019).
5. What Remains to be Done

While combatting the spread of substandard and falsified antimalarials and medicines at large is a lofty goal, Nigeria has shown that meaningful progress can be made. As expected, there are some limitations to Nigeria’s approach, and the countermeasures NAFDAC has put in place are not expected to have the same effects for each and every other country in sub-Saharan Africa. However, Nigeria’s overarching strategy provides an excellent springboard upon which other countries can create their own personalized approach to solving this problem. Governments within sub-Saharan Africa should be encouraged to undertake drug regulatory reforms similar to those in Nigeria, yet adapted to fit their specific needs. It is important to understand that manufacturers, importers, wholesalers, prescribers, and pharmacists are all part of the pharmaceutical supply chain, and each needs regulation and transparency to ensure that counterfeits cannot enter at their level (Cohen et al., 2007).

Here, we will touch on how technology, policy, and vigilance are all interconnected and play important roles, regardless of the country or region affected.

Technology

As far as technology has come in recent decades in the anti-counterfeiting domain, there still remain major technological gaps for drug testing and efficient enforcement of quality standards. While there are ample technologies used for these purposes in higher-income countries, these are not transferable to low- and middle-income countries for many reasons. Many of these technologies are too expensive, and costs are further multiplied by the need for consumables. These instruments also typically involve significant training on behalf of the user, which creates another hurdle to effective implementation. In 2016, the literacy rate in sub-Saharan Africa was estimated to be 64% among individuals over 15 years of age, which means that devices must be easy to use with little-to-no training, reading, or writing involved (The World Bank, “Literacy rate, adult total (% of people ages 15 and above)).

New tools need to be created that are optimized for the challenges of low-resource settings – namely, tools that are low-cost, portable, robust, modular (consisting of replaceable and, ideally, off-the-shelf components), and user-friendly (regardless of language spoken by or education level of the user). More specifically, there remains a need for a device capable of detecting poor-quality medicines, without destroying them, throughout the supply chain. While the use of 2D barcodes is helpful at the consumer level, it is not available for wholesalers, distributors, or retailers due to the scratch-off feature. A component that allows for repeated verification at multiple points in time and place is required.

Another technology to consider is one that places more power in the hands of the consumer, allowing patients to verify the legitimacy of a given pharmaceutical at point-of-sale. For this
purpose, we have visualized an application for mobile phones that would do exactly that. This application would allow patients to identify local pharmacies that have specific medications needed while also displaying each pharmacy’s rating. Ratings would be based on what percentage of medicines in stock have been verified by an objective third party, whether it be Sproxil, mPedigree, law enforcement, or another trustworthy regulatory body. Pharmacies would be given anywhere between one and three stars – one being the lowest, three being the highest. One star would indicate that fewer than 50% of medicines have been verified by an external source; two stars, between 50% and 85% of medicines have been verified; three stars, more than 85% of medicines have been verified. Once patients have chosen a pharmacy – ideally, a pharmacy that has both the medicine(s) needed and a three-star rating – the patient could use another feature within the application to verify the drug at the point of sale using the 2D barcode. Immediately upon inputting the code, the app would display if the drug was verified, by whom, and the expiration date.

![Figure 1. Visualization of Mobile Phone Application](image)

While there is ample potential for technologies to be brought to bear in the fight against SF pharmaceuticals, one of the problems lies in the fact that very few are brought to scale such that entire countries or regions can secure their supply chains. No tool, technique, or phone application is of much value if not backed by good governance, at which point significant policy reforms are needed.

**Policy**

As policy relates to technology, there is much that can be done to bring anti-counterfeiting technologies to scale. The mass serialization of pharmaceutical products at the unit-of-sale level
using 2D barcodes would allow pharmacists and patients to verify drug authenticity. These technologies already exist and are in use in select regions, but their potential will remain unrealized without accompanying policy reforms.

There is also growing consensus that there must be an internationally uniform system for tracking and tracing legitimate pharmaceuticals, similar to mPedigree. This would allow for anyone who comes into contact with a given drug, whether it be a manufacturer, distributor, medical professional, consumer, or law enforcement agency, to trace the transaction history, making it easier to identify SF pharmaceuticals and more difficult for counterfeiters to hide the drug’s origin. Policy could require the creation and maintenance of electronic pedigrees to improve supply chain regulation and surveillance efforts.

Separate from technology, yet intertwined, governing policy must evolve with newer forms of commerce in the age of the Internet. With the growth of Internet pharmacies, it has become increasingly complicated to monitor drugs that enter a country. Regulatory reform must extend to these Internet sources as well.

Lastly, continued efforts are needed in both policy and law to stigmatize drug counterfeiting and leverage punishment in proportion to harm caused.

A Need for Vigilance

Making SF medicines a continual topic of discussion in the public space is key. Very few people are aware of the danger in using fraudulent medications, despite the irreversible consequences. Education must be four-pronged – individuals must be taught the consequences of using substandard or falsified drugs, how to identify these drugs, how to report them to the appropriate authorities, and how and where to source legitimate medications. Individuals must remain watchful. In fact, this is the origin of the phrase “Shine your eyes” – a colloquial phrase that was repurposed by NAFDAC’s public awareness campaign in an effort to remind people to stay vigilant, be careful about where they source their medication, and look out for their neighbor’s safety at the same time. If all individuals remain aware of the grim reality of SF medicines and how they can protect themselves and their neighbors, even in seemingly small ways, this makes for a hyper-vigilant society, at which point significant impacts can be made.

Further Recommendations

Our findings from a review of the literature and stakeholder interviews allow us to suggest recommendations to individual countries, host governments, and multilateral agencies to decrease the prevalence of SF medicines in sub-Saharan Africa. Recommendations are detailed in Table 1 below.
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<tr>
<th>Recommendation</th>
<th>Notes</th>
<th>Priority</th>
<th>Costs and Risks of Implementation</th>
<th>Location in Supply Chain</th>
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| **Use serialized codes**        | • A process that enables consumers to immediately authenticate product using a 2D barcode on devices/systems already in use  
• Bar code is masked by a scratch-off feature, making it easy to determine if the code has been tampered with further upstream  
**Limitations:**  
• Codes can only be used once due to scratch-off feature  
• Consumers must have mobile phones and connectivity  
• Test is not available for wholesalers, distributors, or retailers due to scratch-off feature                                                                                                                                                                                                                                                                                       | **High** | **Low**                          | At individual            |
| **Increase consumer awareness** of substandard and falsified medicines | • Can reduce the number of consumers who are defrauded  
• Empower the public through local and national media by making this a topic of discussion in the public space                                                                                                                                                                                                                                                                                                                                 | **High** | **Low**                          | At national and individual levels |
| **Educate pharmacists**         | • Pharmacists are the last POC before medicines are given to patients and are presumed experts  
• There is a significant need to add to educational requirements for pharmacists as they are currently not trained on SF medicines  
• Implement new curriculum that focuses on danger of SF medicines and how to identify/report them when found in stock                                                                                                                                                                                                                                                                               | **High** | **Medium**                      | At national and individual levels |
| **Authenticate products**        | **distributed within country**  
• Require drugs that have been authorized by appropriate regulatory bodies to carry a registration number  
• Enables pharmacists and consumers to readily identify whether a medication has been verified, and by whom                                                                                                                                                                                                                                                                                  | **Medium** | **High**                         | At national level          |
| **Engage source economies**     | • Can reduce or inhibit the supply of illegal goods imported into the country  
• Establish trade and health negotiations allowing for random inspections of manufacturing plants in producing countries and pre-inspections of products before export                                                                                                                                                                                                                                                  | **Low**  | **High**                         | At source                 |

**Limitations:**  
• Clandestine or smuggled product can still slip through the export and import detection and deterrence programs  
• Heavy reliance on efficacy and cooperation of source countries  
• Does not address domestically produced products
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| **Support and strengthen enforcement with more prosecutions and stronger punishment** | • Criminal prosecutions become a more effective deterrent for fraudsters as they are more vigorously pursued  
• Consider more severe punishments, including life imprisonment and prohibitively high fineslifetime imprisonment and prohibitive fines | Medium   | High                              | At national level        |
| **Limitations:**                                            | • Due to profit opportunity, there are countless potential criminals that require significant effort to find and prosecute  
• Enforcement resources are limited even in higher-income countries, much less in low-income countries where this trade is prevalent  
• May be a lack of political will to support increased funding for expanded enforcement |          |                                   |                          |
| **Conduct inspections of domestic manufacturing sites as needed** | • Grant power to a regulatory body to: (1) conduct both routine and surprise inspections, as well as inspections upon receiving complaints, (2) conduct raids, and (3) close down all unregistered premises and open drug markets | Low      | High                              | At the national level    |
| **Limitations:**                                            | • This approach requires significant financial and human resources to successfully implement  
• Can be considered to be too militaristic of an approach, which may negatively impact the public’s perception |          |                                   |                          |
| **Regulate the primary supply chain in an attempt to create a well-defined, primary, traditional market** | • Strengthen wholesale and retail medicine distribution system by: (1) creating a central medicine distribution network of warehouses, (2) allowing only registered pharmacies to sell medicines, and (3) allowing only certified pharmacists to dispense product  
• Deter sellers who risk losing certificates by knowingly selling substandard or falsified products | Medium   | High                              | At the national level    |
| **Limitations:**                                            | • There will remain significant demand for low-priced products that fall outside of the primary supply chain due to many patients' inability to afford legitimate medicines available  
• As much as supply chains can be regulated, there will always remain potential for SF products to penetrate them when there is high need and high demand for lifesaving drugs |          |                                   |                          |
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| Safeguard imports                      | • Ban importation of any and all drugs apart from those arriving at specific points of entry, and implement tighter and more effective surveillance at these points  
• Distribute devices to customs officials (e.g., Minilabs, TruScan) allowing for onsite testing of drugs without the need to send them to a central laboratory | High     | Medium / High                     | At border                    |
| Create and maintain electronic pedigree showing transaction history for each package | • Allow manufacturers and regulators to monitor the supply chain, pinpointing the weak points where counterfeits are entering the system | Low      | Medium / High                     | At national and individual levels |
6. Conclusion

Though assessing the true scale and measurable impact substandard and falsified antimalarials have on sub-Saharan Africa is difficult, it is clear that these medicines pose a substantial health and economic problem. SF antimalarials jeopardize tremendous progress and investments made in combatting malaria, calling for a concerted global effort to secure the supply chain, increase quality control, and improve surveillance. Despite the repercussions of this trade on human health and economics, the international and national policies touching on this have typically been inadequate or nonexistent, even in the countries that need them the most. Concurrent interventions and a multipronged approach are needed – nobody can tackle this by themselves.

Fundamentally, SF medicines become an international problem when these products move across borders. This can affect an otherwise cordial relationship between neighboring countries, potentially leading to instability in some regions. At the national level, regulation and policy are necessary but insufficient conditions to control SF drugs. Once put in place, there must be support mechanisms to enforce regulations at the local, regional, and national level. Multiple stakeholders should be involved, from manufacturers to transporters to pharmacists to consumers themselves; either as individual entities or through organized coalitions. Non-governmental organizations also have a role to play; often, their mandate allows insight into global as well as local circumstances that can help inform policy making. And, with so many stakeholders with seats at the table, the ability to use technology to both communicate and address the issue becomes of paramount importance. In limited resource settings, technology can help maximize those resources by identifying key trends in data that can inform decisionmaking at a national level, as well as address immediate concerns. However, this can only work if there is a cohesive goal that every stakeholder deems important.

While Nigeria provides a positive case study that can be used as a model for other countries in sub-Saharan Africa, that is all it is meant to be – a model. There is no one standard solution that applies to all countries. Each country within sub-Saharan Africa has varying inputs into the model, whether it be a different degree of dependency on domestic and overseas manufacturing, different distributors, different education thrusts, different definitions of “counterfeit”, different penalties for those criminals caught in the trade, different technologies available, … the list goes on. And while it would be easy to argue for implementing all proposed solutions simultaneously, each of these interventions necessitates significant financial and human resources, both of which are typically lacking in low- to middle-income malaria-endemic countries. Therefore, each country has to develop policies based on its own situation, infrastructure, and resources.

The hope is that this report may raise awareness of this important research area and encourage further work in this domain.
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